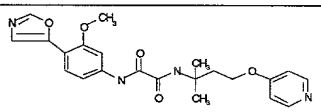
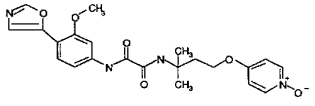
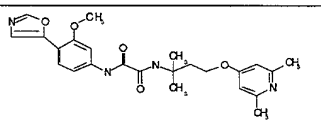
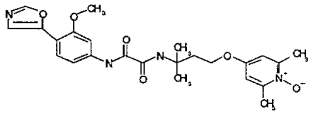
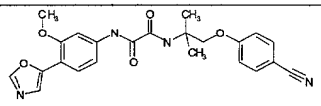
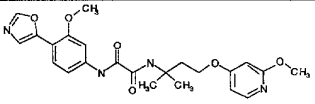
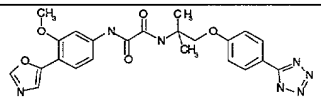
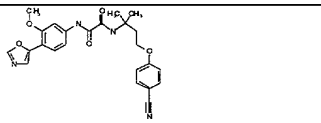
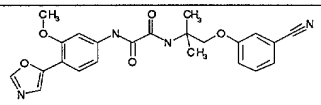
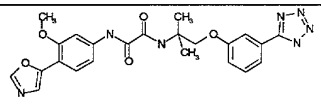
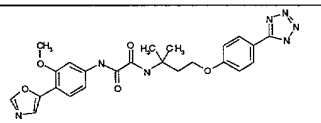
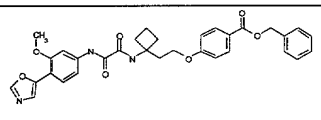
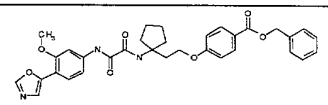
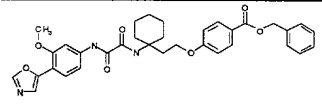
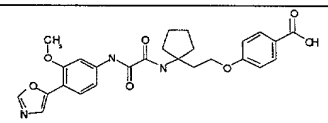
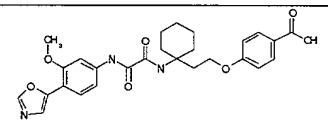
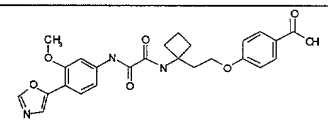
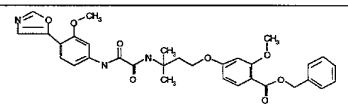
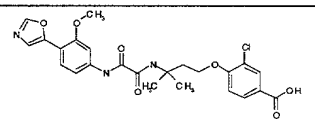
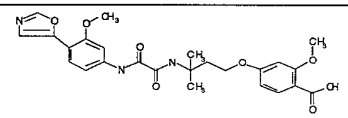
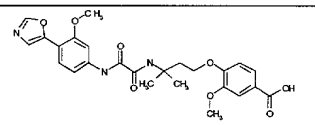
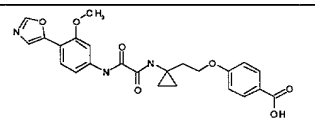
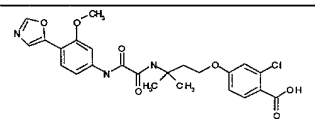
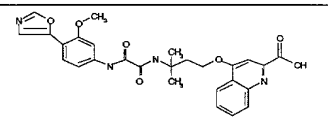
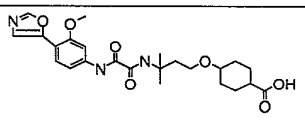
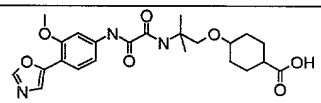
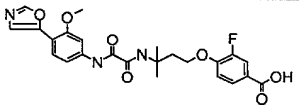
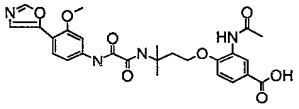
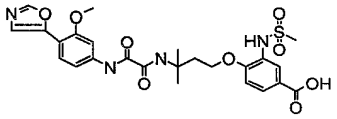
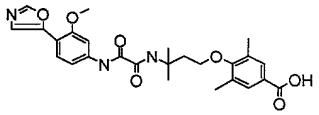
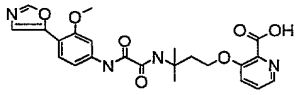
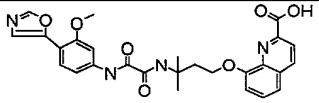
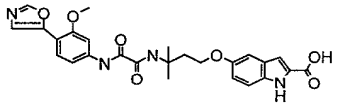
| | | | |
|---|---|---|---|
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-pyridyloxy)propyl]oxalamide |  | 425 | 579 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-3-(1-oxido-4-pyridyloxy)propyl] oxalamide |  | 441 | 580 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-3-(2,6-dimethyl-4-pyridyloxy)propyl] oxalamide |  | 453 | 581 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-3-(2,6-dimethyl-1-oxido-4-pyridyloxy) propyl]oxalamide |  | 469 | 582 |
| N-[2-(4-Cyanophenoxy)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 435 | 583 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[3-(2-methoxy-4-pyridyloxy)-1,1-dimethylpropyl] oxalamide |  | 455 | 584 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-2-[4-(1H-tetrazol-5-yl)phenoxy]ethyl] oxalamide |  | 478 | 585 |
| N-[3-(4-Cyanophenoxy)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 449 | 586 |
| N-[2-(3-Cyanophenoxy)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 476 | 587 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-2-[3-(1H-tetrazol-5-yl)phenoxy]ethyl] oxalamide |  | 478 | 588 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-3-[4-(1H-tetrazol-5-yl)phenoxy]propyl] oxalamide |  | 492 | 589 |
| Benzyl 4-[2-[1-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclobutyl]ethoxy]benzoate |  | 570.2 | 590 |

| | | | |
|---|---|---|---|
| Benzyl 4-[2-[1-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclopentyl]ethoxy]benzoate |  | 584.3 | 591 |
| Benzyl 4-[2-[1-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclohexyl]ethoxy]benzoate |  | 598.3 | 592 |
| 4-[2-[1-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclopentyl]ethoxy]benzoic acid |  | 494.2 | 593 |
| 4-[2-[1-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclohexyl]ethoxy]benzoic acid |  | 508.2 | 594 |
| 4-[2-[1-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl)amino]-1-cyclobutyl]ethoxy]benzoic acid |  | 480.2 | 595 |
| Benzyl 2-methoxy-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoate |  | 588 | 635 |
| 3-Chloro-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid |  | 502 | 636 |
| 2-Methoxy-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid |  | 498 | 637 |
| 3-Methoxy-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid |  | 498 | 638 |
| 4-[2-[1-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-1-cyclopropyl]ethoxy]benzoic acid |  | 466 | 639 |
| 2-Chloro-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid |  | 502 | 640 |
| 4-[3-[[[3-Methoxy-4-(5-oxazolyl) anilino]oxalyl]amino]-3-methylbutoxy]-2-quinolinecarboxylic acid |  | 519 | 641 |

| | | | |
|---|---|---|---|
| (cis/trans)-4-[3-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]-1-cyclohexanecarboxylic acid |  | 474 | 642 |
| (cis/trans)-4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropoxy]-1-cyclohexanecarboxylic acid |  | 460 | 643 |
| 3-Fluoro-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid |  | 486 | 644 |
| 3-Acetamido-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid |  | 525 | 645 |
| 3-(Methanesulfonamido)-4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutoxy]benzoic acid |  | 561 | 646 |
| 4-[3-[[[3-Methoxy-4-(5-oxazolyl) anilino]oxalyl]amino]-3-methylbutoxy]-3,5-dimethylbenzoic acid |  | 496 | 647 |
| 3-[3-[[[3-Methoxy-4-(5-oxazolyl) anilino]oxalyl]amino]-3-methylbutoxy]-2-pyridinecarboxylic acid |  | 469 | 648 |
| 8-[3-[[[3-Methoxy-4-(5-oxazolyl) anilino]oxalyl]amino]-3-methylbutoxy]-2-quinolinecarboxylic acid |  | 519 | 649 |
| 5-[3-[[[3-Methoxy-4-(5-oxazolyl) anilino]oxalyl]amino]-3-methylbutoxy]-2-indolecarboxylic acid |  | 507 | 650 |

Examples 615-631 and 664-670

Example 615

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide.

(i) A mixture of 2g (17.7 mmol) of 2,4,4-trimethyl-2-oxazoline and 1.95 g (17.7 mmol) of thiophenol were heated at 120C for 18 hours. After cooling the resulting solid was triturated

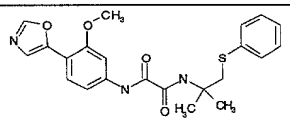
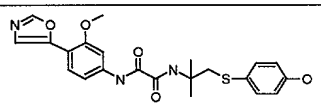
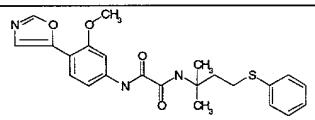
with diethyl ether/petrol (1:2) and filtered off to give 2.55 g of N-[1,1-dimethyl-2-(phenylthio)ethyl]acetamide as a white solid.

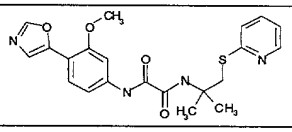
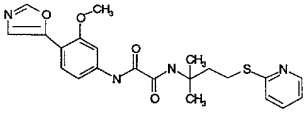
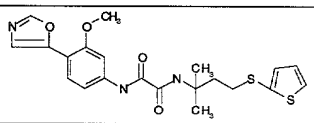
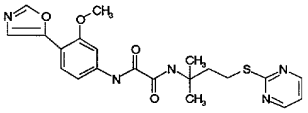
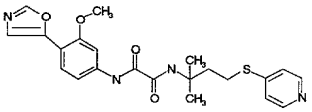
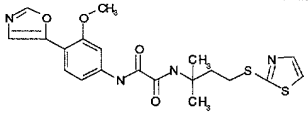
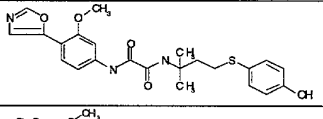
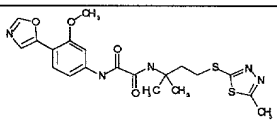
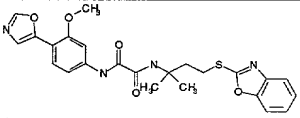
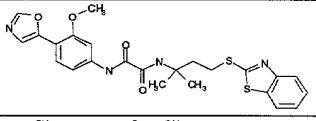
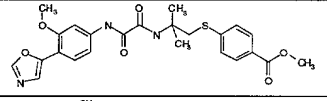
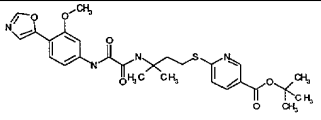
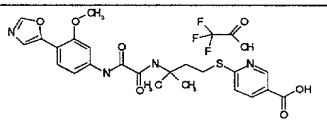
(ii) A solution of 2.5 g (11.2 mmol) of N-[1,1-dimethyl-2-(phenylthio)ethyl]acetamide, 3.18 g (11.2 mmol) of titanium isopropoxide and 3.09 g (16.8 mmol) of diphenylsilane in 12 ml of tetrahydrofuran were stirred at room temperature for 18 hours. The resulting mixture was chromatographed on silica gel using 3%, 6% and 10% methanol in dichloromethane for the elution. There was obtained 2 g of 1,1-dimethyl-2-(phenylthio)ethylamine as a pale orange oil. The 1,1-dimethyl-2-(phenylthio)ethylamine was then coupled to N-[3-methoxy-4-(5-oxazoyl)phenyl oxalamic acid by a procedure analogous to that described in example 1 to afford N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide. MS: m/e 426 $[M+H]^+$.

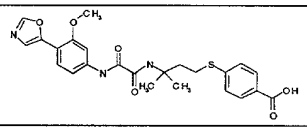
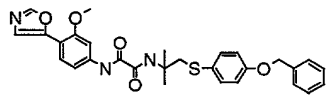
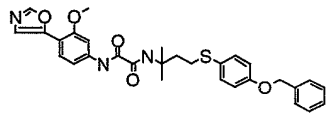
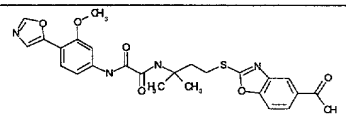
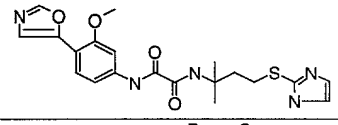
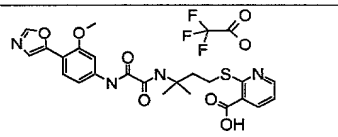
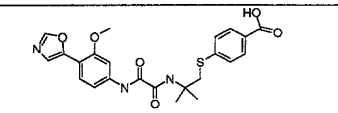
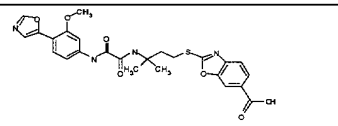
Example 616 was prepared by an analogous method to that described for example 615 but using 4-benzyloxythiophenol in place of the thiophenol and removing the protecting group using a mixture of hydrogen bromide in acetic acid.

The additional compounds in table 1f[2] were prepared in an analogous manner to that described for example 615 by reaction of the appropriate thiol with either 2,4,4-trimethyl-2-oxazoline or 2,4,4-trimethyl-5,6-dihydro-1,3(4H)oxazine and, where necessary, removal of any protecting groups by conventional methods.

table 1f[2]

| Name | Structure | MS(ES) $(M+H)^+$ | Ex No |
|---|---|---|---|
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide |  | 426 | 615 |
| N-[2-(4-Hydroxyphenylthio)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 442 | 616 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide |  | 440 | 617 |

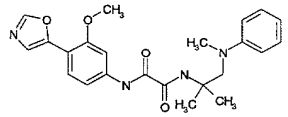
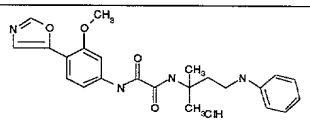
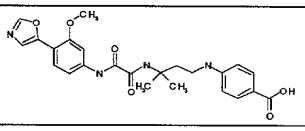
| | | | |
|---|---|---|---|
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-2-(2-pyridylthio)ethyl]oxalamide |  | 427 | 618 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-3-(2-pyridylthio)propyl]oxalamide |  | 441 | 619 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-3-(2-thienylthio)propyl]oxalamide |  | 446 | 620 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-3-(2-pyrimidylthio)propyl]oxalamide |  | 442 | 621 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-3-(4-pyridylthio)propyl]oxalamide |  | 441 | 622 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-3-(2-thiazolylthio)propyl]oxalamide |  | 447 | 623 |
| N-[3-(4-Hydroxyphenylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 456 | 624 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-3-(5-methyl-1,3,4-thiadiazol-2-ylthio) propyl]oxalamide |  | 462 | 625 |
| N-[3-(2-Benzooxazolylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 481 | 626 |
| N-[3-(2-Benzothiazolylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 497 | 627 |
| Methyl 4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropylthio]benzoate |  | 484 | 628 |
| tert-Butyl 6-[3-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-3-methylbutylthio]-3-pyridinecarboxylate |  | 541 | 629 |
| 6-[3-[[[3-Methoxy-4-(5-oxazolyl) anilino]oxalyl]amino]-3-methylbutylthio]-3-pyridinecarboxylic acid trifluoroacetate (1:1) |  | 485 | 630 |

| | | | |
|---|---|---|---|
| 4-[3-[[[3-Methoxy-4-(5-oxazolyl) anilino]oxalyl]amino]-3-methylbutylthio]benzoic acid |  | 484 | 631 |
| N-[2-(4-Benzyloxyphenylthio)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 532 | 664 |
| N-[2-(4-Benzyloxyphenylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 546 | 665 |
| 2-[3-[[[3-Methoxy-4-(5-oxazolyl) anilino]oxalyl]amino]-3-methylbutylthio]-5-benzoxazolecarboxylic acid |  | 525 | 666 |
| N-[3-(1H-Imidazol-2-ylthio)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 430 | 667 |
| 2-[3-[[[3-Methoxy-4-(5-oxazolyl) anilino]oxalyl]amino]-3-methylbutylthio]-3-pyridinecarboxylic acid trifluoroacetate (1:1) |  | 485 | 668 |
| 4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropylthio]benzoic acid |  | 470 | 669 |
| 2-[3-[[[3-Methoxy-4-(5-oxazolyl) anilino]oxalyl]amino]-3-methylbutylthio]-6-benzoxazolecarboxylic acid |  | 525 | 670 |

Examples 632-634

The compounds in table 1f[3] were prepared in an analogous manner to that described for example 398 in table 1f[1] by replacing the 4-nitrophenol with the appropriate aniline and reaction with either 2,4,4-trimethyl-2-oxazoline or 2,4,4-trimethyl-5,6-dihydro-1,3(4H)oxazine and, where necessary, removal of any protecting groups by conventional methods.

table 1f[3]

| Name | Structure | MS(ES) $(M+H)^+$ | Ex No |
|---|---|---|---|
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-2-(N-methylanilino) ethyl] oxalamide |  | 423 | 632 |
| N-(3-Anilino-1,1-dimethylpropyl)-N'-[3-methoxy-4-(5-oxazolyl) phenyl]oxalamide hydrochloride (1:1) |  | 423 | 633 |
| 4-[3-[[[3-Methoxy-4-(5-oxazolyl) anilino]oxalyl]amino]-3-methylbutylamino]benzoic acid |  | 467 | 634 |

***Examples 407-414 ; 459-541 and 651-652***

Typical methods used for the preparation of the compounds of table 1g are described below:

Example 408.

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(4-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide.

(i) A stirred solution of 3.23 g (16.8 mmol) of 1-(4-methoxyphenyl)piperazine, 2.00 g (16.8 mmol) of 2-methyl-2-nitropropan-1-ol and 5.34 g (50.4 mmol) of sodium carbonate in 40ml of n-butanol was refluxed for 16h. The reaction mixture was allowed to cool and diluted with 100ml of dichloromethane. The solution was filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel using petroleum ether/ethyl acetate (10:1) for the elution to afford 1.86 g (6.34 mmol, 38%) of 1-(4-methoxyphenyl)-4-(2-methyl-2nitropropyl)piperazine as a white solid.

(ii) A solution of 1.86 g (6.34 mmol) of 1-(4-methoxyphenyl)-4-(2-methyl-2-nitropropyl)piperazine and 0.5 g of palladium on activated charcoal in 50 ml of ethanol was stirred at room temperature under an atmosphere of hydrogen for 48h. The reaction mixture was filtered and the filtrate concentrated in vacuo to afford 1.59 g (6.04 g mmol, 95%) of 2-[4-(4-methoxyphenyl)-piperazin-1-yl)-1,1-dimethylethylamine as a clear oil. The 2-[4-(4-methoxyphenyl)-piperazin-1-yl)-1,1-dimethylethylamine was then coupled to N-[3-methoxy-4-(5-oxazoyl)phenyl oxalamic acid by a procedure analogous to that described in example 1 to

afford N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(4-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide as a white solid. MS: m/e 508 $[M+H]^+$.

Examples 407, 409, 410, 411, 412 and similar structures were prepared by an analogous procedure by replacing the 1-(4-methoxyphenyl)piperazine with the appropriately substituted piperazine.

Examples 413 and 414 were prepared by an analogous procedure by replacing the 1-(4-methoxyphenyl)piperazine with t-butyl-1-piperazinecarboxylate to give 4-(2-amino-2-methylpropyl)piperazine-1-carboxylic acid t-butyl ester which was then coupled to N-[3-methoxy-4-(5-oxazoyl)phenyl oxalamic acid. The resulting product could then be deprotected to give N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(1-piperazinyl)ethyl]oxalamide that could be used for the preparation of examples 413 , 414 and a variety of additional N-acyl and N-sulfonyl derivatives, such as those shown in table 1g, by using the appropriate acylating or sulfonylating reagent.

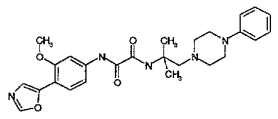
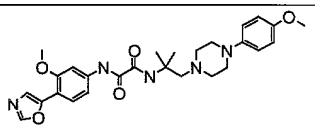
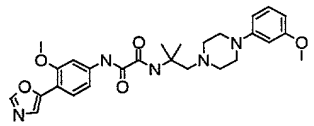
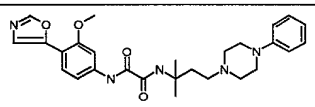
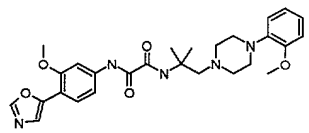
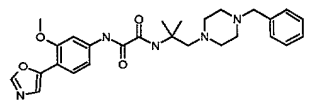
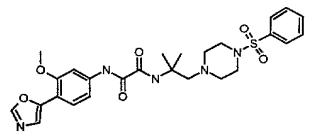
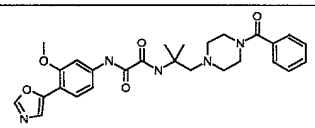
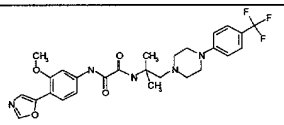
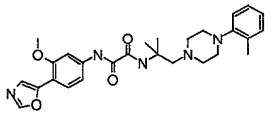
Example 489.

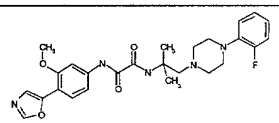
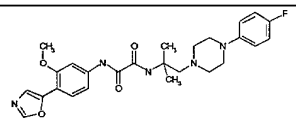
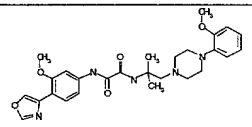
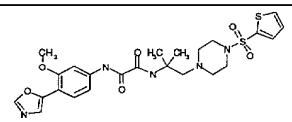
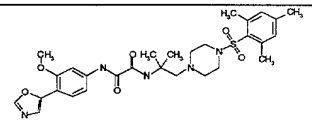
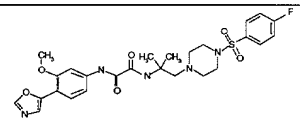
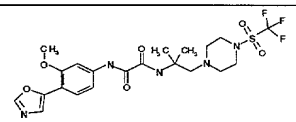
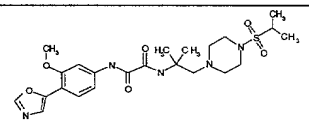
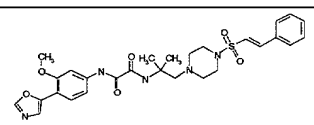
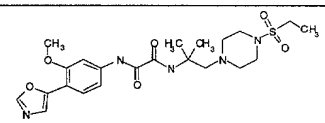
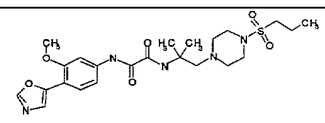
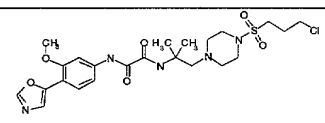
N-[2-[4-(Cyclohexylmethyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide.

A stirred solution of 48mg of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(1-piperazinyl)ethyl]oxalamide (1.2mmol) and 13mg of cyclohexanecarboxaldehyde (1.2mmol) in 1ml of a 5% acetic acid / dichloromethane mixture was treated with a solution of 38mg of sodium triacetoxyborohydride (1.8mmol) in 1ml of a 5% acetic acid / dichloromethane mixture. After stirring overnight at room temperature the reaction mixture was diluted with 10ml of dichloromethane and washed with 8ml of a sodium bicarbonate solution followed by 8ml of water. The organic layer was then evaporated and purified using flash chromatography on a silica gel column eluting with 5% methanol / dichloromethane to give after evaporation of the fractions 14.3mg (0.3 mmol, 25%) of N-[2-[4-(cyclohexylmethyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide in the form of a white solid. MS: m/e 498.2 $[M+H]^+$.

Additional N-alkylated compounds shown in table 1g were prepared by analogous methods.

table 1g

| Name | Structure | MS(ES) $(M+H)^+$ | Ex No |
|---|---|---|---|
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-phenyl-1-piperazinyl)ethyl]oxalamide |  | 478 | 407 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(4-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide |  | 508 | 408 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide |  | 508 | 409 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-3-(4-phenyl-1-piperazinyl)propyl]oxalamide |  | 492 | 410 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(2-methoxy-phenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide |  | 508 | 411 |
| N-[2-(4-Benzyl-1-piperazinyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 492 | 412 |
| N-[2-[4-(Benzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 452 | 413 |
| N-[2-(4-Benzoyl-1-piperazinyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 506 | 414 |
| N-[2-[4-[4-(Trifluoromethyl)phenyl]-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 546 | 459 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]oxalamide |  | 492 | 460 |

| | | | |
|---|---|---|---|
| N-[2-[4-(2-Fluorophenyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 496 | 461 |
| N-[2-[4-(4-Fluorophenyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 496 | 462 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide |  | 508 | 463 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-thiophenesulfonyl)-1-piperazinyl]ethyl]oxalamide |  | 548 | 464 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2,4,6-trimethylbenzenesulfonyl)-1-piperazinyl]ethyl]oxalamide |  | 584.1 | 465 |
| N-[2-[4-(4-Fluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 560.1 | 466 |
| N-[2-[4-(Trifluoromethanesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl)]oxalamide |  | 534 | 467 |
| N-[2-[4-(Isopropylsulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl)]oxalamide |  | 508.1 | 468 |
| (E)-N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(styrylsulfonyl)-1-piperazinyl]ethyl]oxalamide |  | 568.1 | 469 |
| N-[2-[4-(Ethanesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 494.1 | 470 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(propanesulfonyl)-1-piperazinyl]ethyl]oxalamide |  | 508.1 | 471 |
| N-[2-[4-(3-Chloropropanesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 542.1 | 472 |

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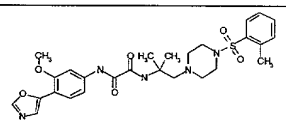
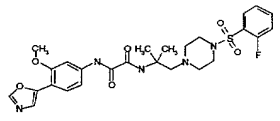
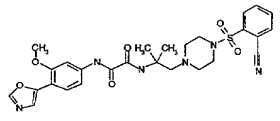
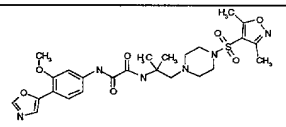
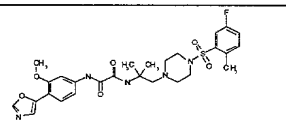
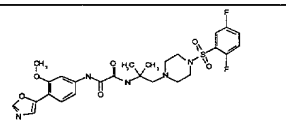
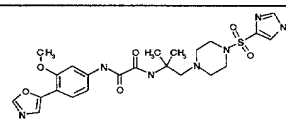
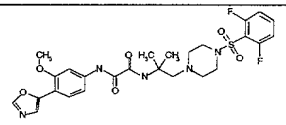
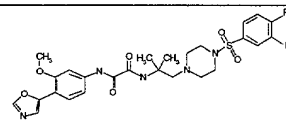
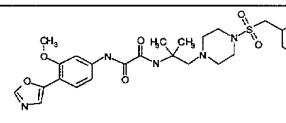
|---|---|---|---|
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(o-toluenesulfonyl)-1-piperazinyl]ethyl]oxalamide |  | 556.1 | 473 |
| N-[2-[4-(2-Fluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 560.1 | 474 |
| N-[2-[4-(2-Cyanobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 567.1 | 475 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3,5-dimethyl-4-isoxazolylsulfonyl)-1-piperazinyl]-1,1-dimethyl-ethyl]oxalamide |  | 561.1 | 476 |
| N-[2-[4-(5-Fluoro-2-methylbenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 574.1 | 477 |
| N-[2-[4-(2,5-Difluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 578.1 | 478 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(1-methyl-1H-imidazole-4-sulfonyl)-1-piperazinyl]ethyl]oxalamide |  | 546.1 | 479 |
| N-[2-[4-(2,6-Difluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 578.1 | 480 |
| N-[2-[4-(3,4-Difluorobenzenesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 578.1 | 481 |
| N-[2-[4-(Cyclohexylmethanesulfonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 562.2 | 482 |

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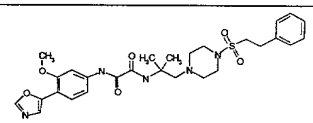
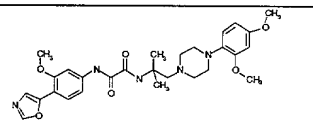
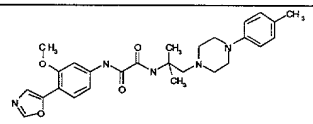
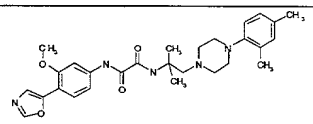
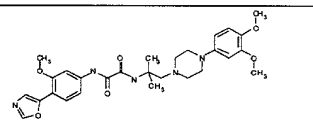
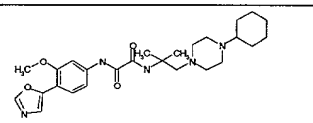
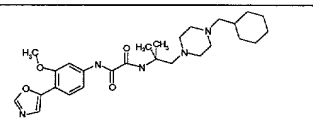
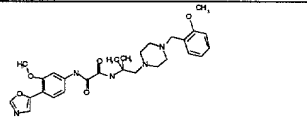
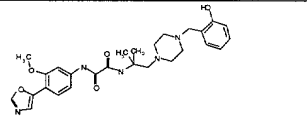
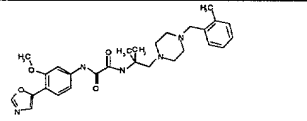
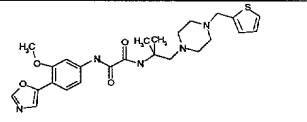
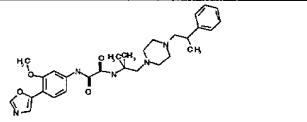
|---|---|---|---|
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-phenylethanesulfonyl)-1-piperazinyl]ethyl]oxalamide |  | 570.1 | 483 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(2,4-dimethoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide |  | 538 | 484 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(4-methylphenyl)-1-piperazinyl]ethyl]oxalamide |  | 492 | 485 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2,4-dimethylphenyl)-1-piperazinyl]ethyl]oxalamide |  | 506 | 486 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3,4-dimethoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide |  | 538 | 487 |
| N-[2-(4-Cyclohexyl-1-piperazinyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 484.4 | 488 |
| N-[2-[4-(Cyclohexylmethyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 498.2 | 489 |
| N-[2-[4-(2-Methoxybenzyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 522.1 | 490 |
| N-[2-[4-(2-Hydroxybenzyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 508.1 | 491 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-methylbenzyl)-1-piperazinyl]ethyl]oxalamide |  | 506.1 | 492 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-thenyl)-1-piperazinyl]ethyl]oxalamide |  | 498.1 | 493 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2(RS)-phenylpropyl)-1-piperazinyl]ethyl]oxalamide |  | 520.2 | 494 |

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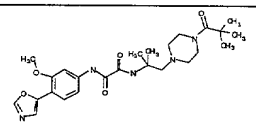
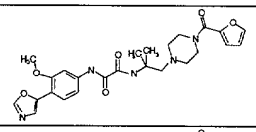
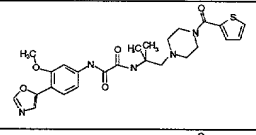
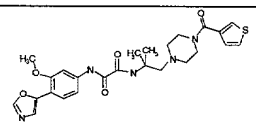
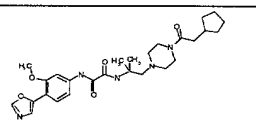
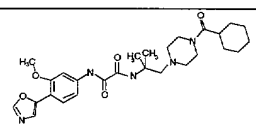
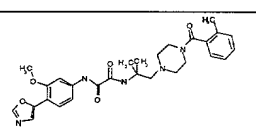
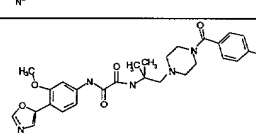
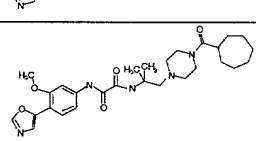
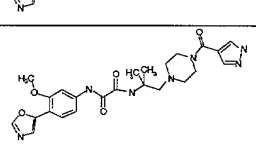
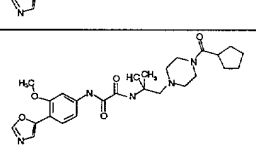
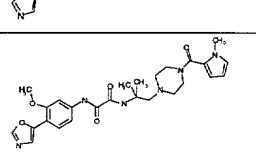
|---|---|---|---|
| N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-pivaloyl-1-piperazinyl)ethyl]oxalamide |  | 486.1 | 495 |
| N-[2-[4-(2-Furoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 496.1 | 496 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-thenoyl)-1-piperazinyl]ethyl]oxalamide |  | 512.1 | 497 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(3-thenoyl)-1-piperazinyl]ethyl]oxalamide |  | 512 | 498 |
| N-[2-[4-(2-Cyclopentylacetyl)-1-piperazinyl]-1,1-dimethyl-ethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl)]oxalamide |  | 512.1 | 499 |
| N-[2-[4-(Cyclohexylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 512.1 | 500 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-methylbenzoyl)-1-piperazinyl]ethyl]oxalamide |  | 520.1 | 501 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(4-methylbenzoyl)-1-piperazinyl]ethyl]oxalamide |  | 520.1 | 502 |
| N-[2-[4-(Cycloheptylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 526.2 | 503 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-]1,1-dimethyl-2-[4-[(1H-pyrazol-4-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide |  | 496.1 | 504 |
| N-[2-[4-(Cyclopentylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 498.1 | 505 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-Dimethyl-2-[4-[(1-methyl-1H-pyrrol-2-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide |  | 509.1 | 506 |

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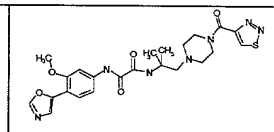
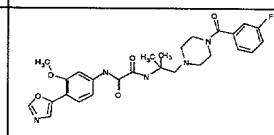
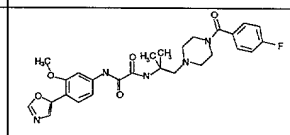
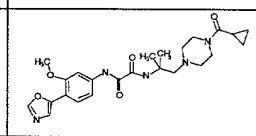
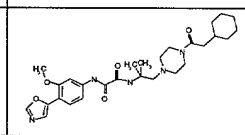
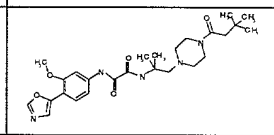
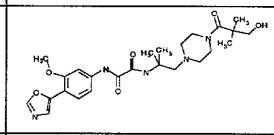
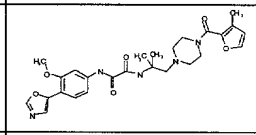
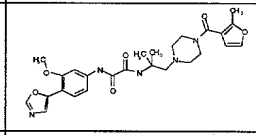
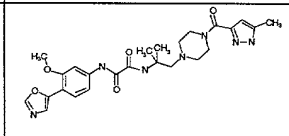
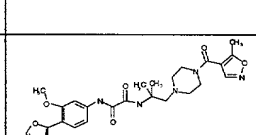
|---|---|---|---|
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(1,2,3-thiadiazol-4-yl)carbonyl]-1-piperazinyl]-ethyl]oxalamide |  | 514.1 | 507 |
| N-[2-[4-(3-Fluorobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 524.1 | 508 |
| N-[2-[4-(4-Fluorobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 524.1 | 509 |
| N-[2-[4-(Cyclopropylcarbonyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 470.1 | 510 |
| N-[2-[4-(2-Cyclohexylacetyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 526.2 | 511 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3,3-dimethylbutyryl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide |  | 500.2 | 512 |
| N-[2-[4-(3-Hydroxy-2,2-dimethylpropionyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 502.1 | 513 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(3-methyl-2-furoyl)-1-piperazinyl]ethyl]oxalamide |  | 510.1 | 514 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-methyl-3-furoyl)-1-piperazinyl]ethyl]oxalamide |  | 510.1 | 515 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-methyl-1H-pyrazol-3-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide |  | 510.1 | 516 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-methyl-4-isoxazolyl)carbonyl]-1-piperazinyl]ethyl]oxalamide |  | 511.1 | 517 |

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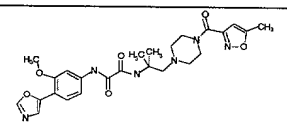
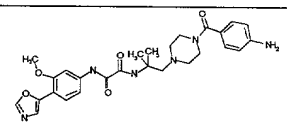
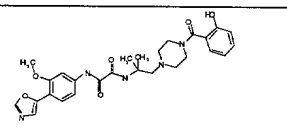
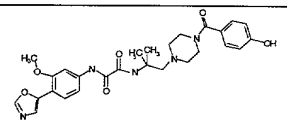
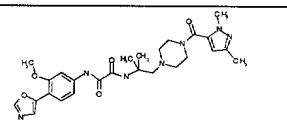
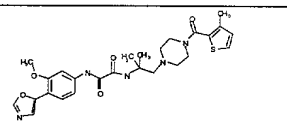
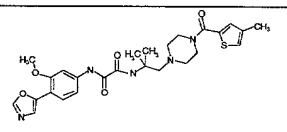
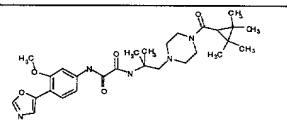
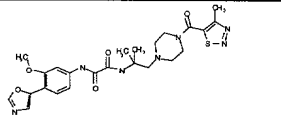
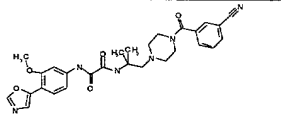
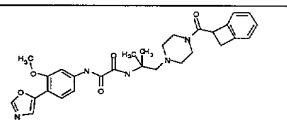
|---|---|---|---|
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(5-methyl-3-isoxazolyl)carbonyl]-1-piperazinyl]ethyl]oxalamide |  | 511.1 | 518 |
| N-[2-[4-(4-Aminobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 521.1 | 519 |
| N-[2-[4-(2-Hydroxybenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 522.1 | 520 |
| N-[2-[4-(4-Hydroxybenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 522.1 | 521 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2,5-dimethyl-2H-pyrazol-3-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide |  | 524.1 | 522 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(3-methyl-2-thenoyl)-1-piperazinyl]ethyl]oxalamide |  | 526.1 | 523 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(4-methyl-2-thenoyl)-1-piperazinyl]ethyl]oxalamide |  | 526.1 | 524 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2,2,3,3-tetramethyl-1-cyclopropyl)carbonyl]-1-piperazinyl]ethyl]oxalamide |  | 526.2 | 525 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(4-methyl-1,2,3-thiadiazol-5-yl)carbonyl]-1-piperazinyl]ethyl]oxalamide |  | 528.1 | 526 |
| N-[2-[4-(3-Cyanobenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 531.1 | 527 |
| N-[2-[4-[(Bicyclo[4.2.0]octa-1(6),2,4-trien-7-yl)carbonyl]-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 532.1 | 528 |

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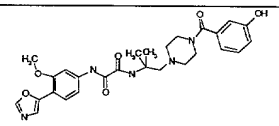
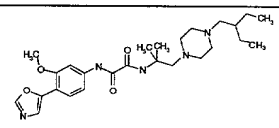
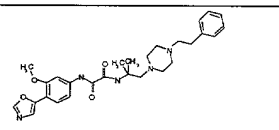
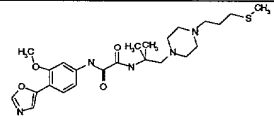
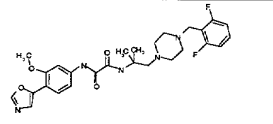
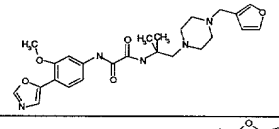
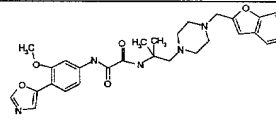
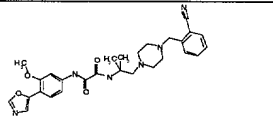
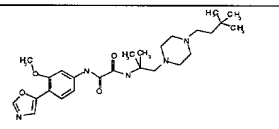
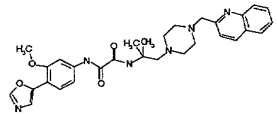
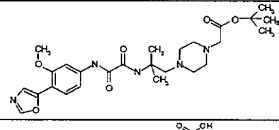
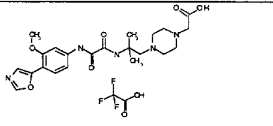
|---|---|---|---|
| N-[2-[4-(3-Hydroxybenzoyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 522.1 | 529 |
| N-[2-[4-(2-Ethylbutyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 486.1 | 530 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-(2-phenylethyl)-1-piperazinyl]ethyl]oxalamide |  | 506.2 | 531 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[3-(methylthio)propyl]-1-piperazinyl]ethyl]oxalamide |  | 490.1 | 532 |
| N-[2-[4-(2,6-Difluorobenzyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 528.1 | 533 |
| N-[2-[4-(3-Furfuryl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 482.1 | 534 |
| N-[2-[4-[(2-Benzofuranyl)methyl]-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl)]oxalamide |  | 532.1 | 535 |
| N-[2-[4-(2-Cyanobenzyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 517.1 | 536 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[2-[4-(3,3-dimethylbutyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide |  | 486.2 | 537 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-[4-[(2-quinolinyl)methyl]-1-piperazinyl]ethyl]oxalamide |  | 543.2 | 538 |
| tert-Butyl 4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-1-piperazineacetate |  | 516 | 539 |
| 4-[2-[[[3-Methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-1-piperazineacetic acid trifluoroacetate (1:1) |  | 460 | 540 |

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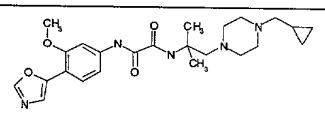
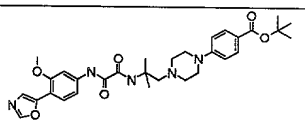
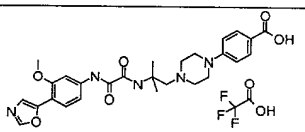
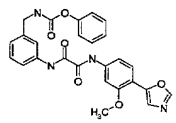
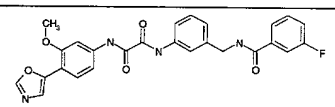
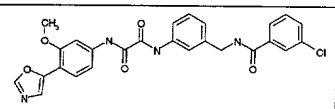
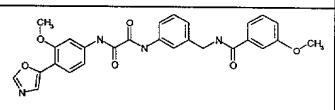
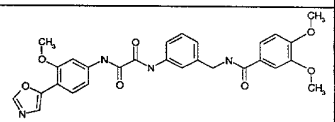
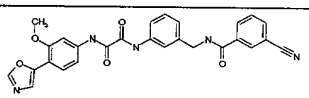
|---|---|---|---|
| N-[2-[4-(Cyclopropylmethyl)-1-piperazinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 456 | 541 |
| tert-Butyl 4-[4-[2-[[[3-methoxy-4-(5-oxazolyl)anilino]oxalyl]amino]-2-methylpropyl]-1-piperazinyl] benzoate |  | 578 | 651 |
| 4-[4-[2-[[[3-Methoxy-4-(5-oxazolyl) anilino]oxalyl]amino]-2-methylpropyl]-1-piperazinyl]benzoic acid trifluoroacetate (1:1) |  | 522 | 652 |

***Examples 415-420:***

In a manner analogous to that described in Example 4 starting with N-[3-(aminomethylphenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide and the appropriate carboxylic acid chloride compounds shown in table 1h were prepared.

table 1h

| Name | Structure | ME(ES) $(M+H)^+$ | Ex No |
|---|---|---|---|
| Phenyl [3-[[[4-(5-oxazolyl)anilino]oxalyl]amino]benzyl] carbamate |  | 487 | 415 |
| N-[3-[(3-Fluorobenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 489 | 416 |
| N-[3-[(3-Chlorobenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 505 | 417 |
| N-[3-[(3-Methoxybenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 501.2 | 418 |
| N-[3-[(3,4-Dimethoxybenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 531.2 | 419 |

| | | | |
|---|---|---|---|
| N-[3-[(3-Cyanobenzamido)methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 496.1 | 420 |

*Examples 421-427 and 598-614 :*

Typical methods used for the preparation of the compounds of table 1b are described below:

Examples 421 and 423 were prepared by reaction of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-piperidinyl)ethyl]oxalamide with the appropriate acylating reagent.

Example 424 was prepared in a manner analogous to that described in Example 1, starting with N-[3-methoxy-4-(5-oxazoyl)phenyl oxalamic acid, prepared as described in Example 1, parts (i) and (ii), and the appropriate amine.

Example 422

N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide.

(i) A mixture of 2g (17.7 mmol) of 2,4,4-trimethyl-2-oxazoline and 1.95 g (17.7 mmol) of thiophenol were heated at 120C for 18 hours. After cooling the resulting solid was triturated with diethyl ether/petrol (1:2) and filtered off to give 2.55 g of N-[1,1-dimethyl-2-(phenylthio)ethyl]acetamide as a white solid.

(ii) A solution of 2.5 g (11.2 mmol) of N-[1,1-dimethyl-2-(phenylthio)ethyl]acetamide, 3.18 g (11.2 mmol) of titanium isopropoxide and 3.09 g (16.8 mmol) of diphenylsilane in 12 ml of tetrahydrofuran were stirred at room temperature for 18 hours. The resulting mixture was chromatographed on silica gel using 3%, 6% and 10% methanol in dichloromethane for the elution. There was obtained 2 g of 1,1-dimethyl-2-(phenylthio)ethylamine as a pale orange oil. The 1,1-dimethyl-2-(phenylthio)ethylamine was then coupled to N-[3-methoxy-4-(5-oxazoyl)phenyl oxalamic acid by a procedure analogous to that described in example 1 to afford N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide. MS: m/e 426 $[M+H]^+$.

Example 427 was prepared by an analogous method to that described for example 422 but using 4-benzyloxythiophenol in place of the thiophenol and removing the protecting group using a mixture of hydrogen bromide in acetic acid.

Example 607 was prepared starting from benzofuran-3-acetic ethyl ester by alkylation iodomethane using potassium tertiary butoxide as base followed by alkaline hydrolysis, Curtius reaction, hydrolysis in ethylene glycol and water at 180°C. The resulting amine was then coupled to N-[3-methoxy-4-(5-oxazoyl)phenyl oxalamic acid as described in Example 1.

Example 426 was prepared in a manner analogous to that described for example 408 in table 1g using tetrahydro quinoline in place of 1-(4-methoxyphenyl)piperazine.

Example 610

N-[2-[1-(Methanesulfonyl)-4-piperidinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide

14 mg (0.12 mmol) of methanesulphonyl chloride were added to a solution of 40 mg (0.1 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl-N'-[1,1-dimethyl-2-(4-piperidinyl)ethyl]oxalamide in 1 ml of dichloromethane followed by 17 mg (0.15 mmol) of N-ethylmorpholine and the mixture stirred at room temperature for 4 hours. The resulting solution was diluted with ethyl acetate, washed with 2M hydrochloric acid and saturated sodium bicarbonate solution, dried over magnesium sulphate, evaporated to dryness and the residue triturated with diethyl ether. There was obtained 23 mg of N-[2-[1-(methanesulfonyl)-4-piperidinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide as an off-white solid. MS m/e 479 $[M+H]^+$.

The starting material was prepared as follows:

i) A solution of 4.65 g (31 mmol) of alpha, alpha-dimethyl-4-pyridineethylamine, 15.6 g (0.154 mol) of triethylamine and 13.5g (61.9 mmol) of di-tert-butyl dicarbonate in 100 ml of methanol was stirred at room temperature for 2 days then evaporated to dryness. The residue

was dissolved in ethyl acetate, washed with water, dried over magnesium sulphate, evaporated to dryness and chromatographed on silica gel using ethyl acetate/petrol (2:1) for the elution. There was obtained 2.12 g of tert-butyl [1,1-dimethyl-2-(4-pyridyl)ethyl]carbamate as a pale orange solid. $^1$H NMR (400 MHz $CDCl_3$) δ: 1.29 (6H,s), 1.49 (9H,s), 3.04 (2H,s), 4.30 (1H, br.s), 7.10 (2H,d), 8.52 (2H,d).

ii) 2.1 g (8.4 mmol) of tert-butyl [1,1-dimethyl-2-(4-pyridyl)ethyl]carbamate, in 20 ml of methanol were hydrogenated with 400 mg of 10% palladium on carbon catalyst at 70°C and 7 Bar for 6 days. The resulting suspension was filtered, evaporated to dryness and the residue triturated with diethyl ether/petrol (1:9) to give 1.2 g of tert-butyl [1,1-dimethyl-2-(4-piperidinyl)ethyl]carbamate as a white solid. $^1$H NMR (400 MHz DMSO) δ: 1.18 (6H,s), 1.28-1.41 (2H,m), 1.37 (9H,s), 1.52-1.69 (3H,m), 1.75-1.83 (2H,d), 2.74-2.84 (2H,t), 3.12-3.21 (2H,d), 6.40-6.48 (1H,br.s), 8.60-8.95 (1H,br.s).

iii) A solution of 1.2 g (4.68 mmol) of tert-butyl [1,1-dimethyl-2-(4-piperidinyl)ethyl]carbamate, 945 mg (9.36 mmol) of triethylamine and 2.33 g (9.36 mmol) of N-(benzyloxycarbonyloxy)succinimide in 20 ml of dichloromethane was stirred at room temperature for 18 hours then washed with 10% citric acid solution and saturated sodium bicarbonate solution. The organic phase was dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/petrol (1:2) for the elution. There was obtained 1.89 g of benzyl 4-[2-(tert-butoxyformamido)-2-methylpropyl]-1-piperidinecarboxylate. $^1$H NMR (400 MHz $CDCl_3$) δ: 1.15-1.32 (2H,m), 1.29 (6H,s), 1.42 (9H,s), 1.49-1.78 (5H,m), 2.75-2.90 (2H,m), 4.05-4.16 (2H,m), 4.41 (1H,br.s), 5.12 (2H,s), 7.27-7.42 (5H,m).

iv) A solution of 1.79 g (4.6 mmol) of benzyl 4-[2-(tert-butoxyformamido)-2-methylpropyl]-1-piperidinecarboxylate in 6 ml of trifluoroacetic acid/dichloromethane (1:1) was stirred at room temperature for 5 minutes then evaporated to dryness. The residue was dissolved in 20 ml of dichloromethane along with 1.2 g (4.58 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid, 1.1 g (5.74 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, 1.32g (11.5 mmol) of N-ethylmorpholine and 1.1 g (6.9mmol) of 1-hydroxy-7-azabenzotriazole. After stirring overnight the solution was diluted with ethyl acetate, washed with 10% citric acid solution and saturated sodium bicarbonate

solution, dried over magnesium sulphate evaporated to dryness and chromatographed on silica gel using ethyl acetate/petrol (1:1) for the elution. There was obtained 1.14 g of benzyl 4-{2-[[[3-methoxy-4-(5-oxazolyl)phenylamino]oxalyl]amino]-2-methylpropyl}-1-piperidinecarboxylate as a white foam. MS: m/e 535 $[M+H]^+$.

v) A solution of 1.1 g (2.05 mmol) of benzyl 4-{2-[[[3-methoxy-4-(5-oxazolyl)phenylamino]oxalyl]amino]-2-methylpropyl}-1-piperidinecarboxylate in 25 ml of methanol was hydrogenated with 100 mg of 10% palladium on carbon catalyst for 4 hours. The resulting suspension was filtered and evaporated to dryness to give 732 mg of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-piperidinyl)ethyl]oxalamide as an off-white solid. MS: m/e 401 $[M+H]^+$.

Example 616 was prepared starting from benzofuran-3-acetic ethyl ester by alkylation iodomethane using potassium tertiary butoxide as base followed by alkaline hydrolysis, Curtius reaction, hydrolysis in ethylene glycol and water at 180°C. The resulting amine was then coupled to N-[3-methoxy-4-(5-oxazoyl)phenyl oxalamic acid as described in Example 1

Example 619

N-[2-[1-(Methanesulfonyl)-4-piperidinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide

14 mg (0.12 mmol) of methanesulphonyl chloride were added to a solution of 40 mg (0.1 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl-N'-[1,1-dimethyl-2-(4-piperidinyl)ethyl]oxalamide in 1 ml of dichloromethane followed by 17 mg (0.15 mmol) of N-ethylmorpholine and the mixture stirred at room temperature for 4 hours. The resulting solution was diluted with ethyl acetate, washed with 2M hydrochloric acid and saturated sodium bicarbonate solution, dried over magnesium sulphate, evaporated to dryness and the residue triturated with diethyl ether. There was obtained 23 mg of N-[2-[1-(methanesulfonyl)-4-piperidinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide as an off-white solid. MS m/e 479 $[M+H]^+$.

The starting material was prepared as follows:

i) A solution of 4.65 g (31 mmol) of alpha, alpha-dimethyl-4-pyridineethylamine, 15.6 g (0.154 mol) of triethylamine and 13.5g (61.9 mmol) of di-tert-butyl dicarbonate in 100 ml of methanol was stirred at room temperature for 2 days then evaporated to dryness. The residue was dissolved in ethyl acetate, washed with water, dried over magnesium sulphate, evaporated to dryness and chromatographed on silica gel using ethyl acetate/petrol (2:1) for the elution. There was obtained 2.12 g of tert-butyl [1,1-dimethyl-2-(4-pyridyl)ethyl]carbamate as a pale orange solid. $^1$H NMR (400 MHz $CDCl_3$) δ: 1.29 (6H,s), 1.49 (9H,s), 3.04 (2H,s), 4.30 (1H, br.s), 7.10 (2H,d), 8.52 (2H,d).

ii) 2.1 g (8.4 mmol) of tert-butyl [1,1-dimethyl-2-(4-pyridyl)ethyl]carbamate, in 20 ml of methanol were hydrogenated with 400 mg of 10% palladium on carbon catalyst at 70°C and 7 Bar for 6 days. The resulting suspension was filtered, evaporated to dryness and the residue triturated with diethyl ether/petrol (1:9) to give 1.2 g of tert-butyl [1,1-dimethyl-2-(4-piperidinyl)ethyl]carbamate as a white solid. $^1$H NMR (400 MHz DMSO) δ: 1.18 (6H,s), 1.28-1.41 (2H,m), 1.37 (9H,s), 1.52-1.69 (3H,m), 1.75-1.83 (2H,d), 2.74-2.84 (2H,t), 3.12-3.21 (2H,d), 6.40-6.48 (1H,br.s), 8.60-8.95 (1H,br.s).

iii) A solution of 1.2 g (4.68 mmol) of tert-butyl [1,1-dimethyl-2-(4-piperidinyl)ethyl]carbamate, 945 mg (9.36 mmol) of triethylamine and 2.33 g (9.36 mmol) of N-(benzyloxycarbonyloxy)succinimide in 20 ml of dichloromethane was stirred at room temperature for 18 hours then washed with 10% citric acid solution and saturated sodium bicarbonate solution. The organic phase was dried over magnesium sulphate, evaporated to dryness and the residue chromatographed on silica gel using ethyl acetate/petrol (1:2) for the elution. There was obtained 1.89 g of benzyl 4-[2-(tert-butoxyformamido)-2-methylpropyl]-1-piperidinecarboxylate. $^1$H NMR (400 MHz $CDCl_3$) δ: 1.15-1.32 (2H,m), 1.29 (6H,s), 1.42 (9H,s), 1.49-1.78 (5H,m), 2.75-2.90 (2H,m), 4.05-4.16 (2H,m), 4.41 (1H,br.s), 5.12 (2H,s), 7.27-7.42 (5H,m).

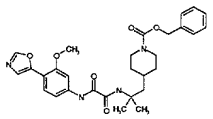
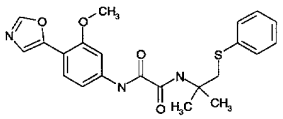
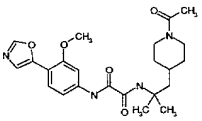
iv) A solution of 1.79 g (4.6 mmol) of benzyl 4-[2-(tert-butoxyformamido)-2-methylpropyl]-1-piperidinecarboxylate in 6 ml of trifluoroacetic acid/dichloromethane (1:1) was stirred at room temperature for 5 minutes then evaporated to dryness. The residue was dissolved in 20 ml of dichloromethane along with 1.2 g (4.58 mmol) of N-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamic acid, 1.1 g (5.74 mmol) of 1-(3-dimethylaminopropyl)-3-

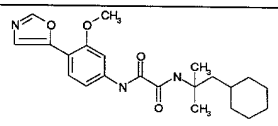
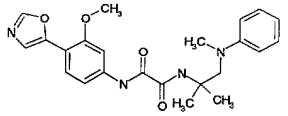
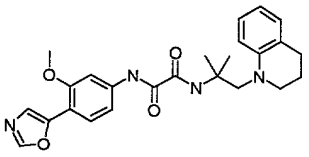
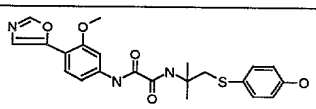
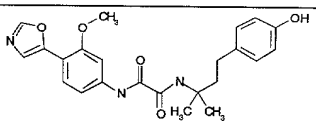
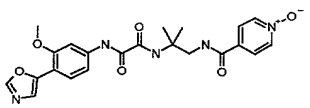
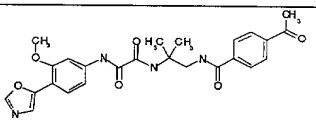
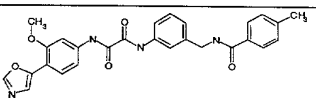
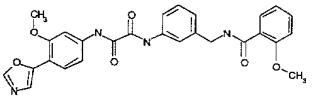
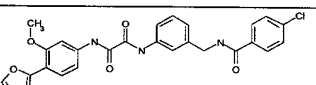
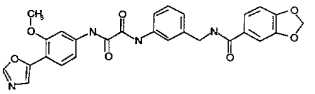
ethylcarbodiimide hydrochloride, 1.32g (11.5 mmol) of N-ethylmorpholine and 1.1 g (6.9mmol) of 1-hydroxy-7-azabenzotriazole. After stirring overnight the solution was diluted with ethyl acetate, washed with 10% citric acid solution and saturated sodium bicarbonate solution, dried over magnesium sulphate evaporated to dryness and chromatographed on silica gel using ethyl acetate/petrol (1:1) for the elution. There was obtained 1.14 g of benzyl 4-{2-[[[3-methoxy-4-(5-oxazolyl)phenylamino]oxalyl]amino]-2-methylpropyl}-1-piperidinecarboxylate as a white foam. MS: m/e 535 $[M+H]^+$.

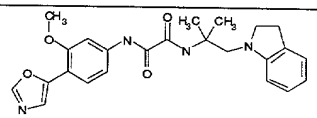
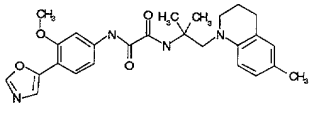
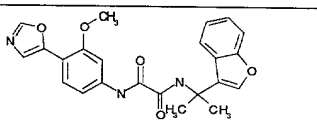
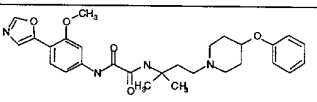
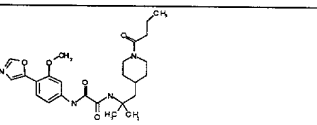
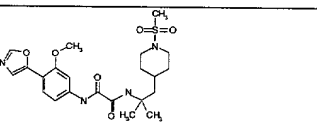
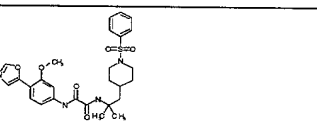
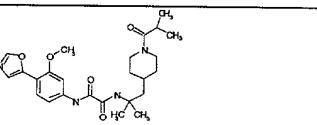
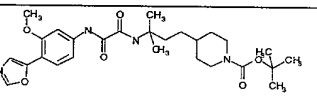
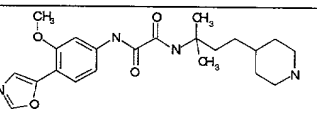
v) A solution of 1.1 g (2.05 mmol) of benzyl 4-{2-[[[3-methoxy-4-(5-oxazolyl)phenylamino]oxalyl]amino]-2-methylpropyl}-1-piperidinecarboxylate in 25 ml of methanol was hydrogenated with 100 mg of 10% palladium on carbon catalyst for 4 hours. The resulting suspension was filtered and evaporated to dryness to give 732 mg of N-[3-methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-piperidinyl)ethyl]oxalamide as an off-white solid. MS: m/e 401 $[M+H]^+$.

The remaining examples in table 1b were prepared by methods analogous to those described above, as appropriate to the structure, or by methods previously described for related structures.

table 1b

| Name | Structure | MS(ES) $(M+H)^+$ | Ex No |
|---|---|---|---|
| Benzyl 4-{2-[[[3-methoxy-4-(5-oxazolyl)phenylamino]oxalyl]amino]-2-methylpropyl}-1-piperidinecarboxylate |  | 535 | 421 |
| N-[3-Methoxy-4-(5-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(phenylthio)ethyl]oxalamide |  | 426 | 422 |
| N-[2-(1-Acetyl-4-piperidinyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 443 | 423 |

| | | | |
|---|---|---|---|
| N-(2-Cyclohexyl-1,1-dimethylethyl)-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 400 | 424 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-2-(N-methylanilino)ethyl]oxalamide |  | 423 | 425 |
| N-[2-(1,2,3,4-Tetrahydro-1-quinolyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl) phenyl]oxalamide |  | 449 | 426 |
| N-[2-(4-Hydroxyphenylthio)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamide |  | 442 | 427 |
| N-[3-(4-Hydroxyphenyl)-1,1-dimethylpropyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamide |  | 424 | 598 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-2-[(1-oxido-4-pyridyl)carboxamido] ethyl]oxalamide |  | 454 | 599 |
| N-[2-(4-Acetylbenzamido)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 479.1 | 600 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[3-[(4-methylbenzamido)methyl]phenyl]oxalamide |  | 485.1 | 601 |
| N-[3-[(2-Methoxybenzamido) methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 501.1 | 602 |
| N-[3-[(4-Chlorobenzmido) methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 505.1 | 603 |
| N-[3-[[(1,3-Benzodioxol-5-yl)carboxamido]methyl]phenyl]-N'-[3-methoxy-4-(5-oxazolyl) phenyl]oxalamide |  | 515.2 | 604 |

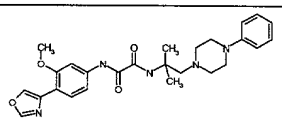
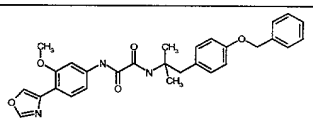
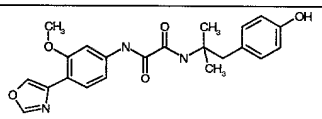
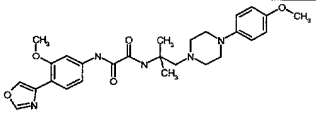
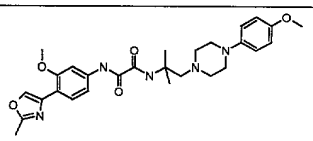
| | | | |
|---|---|---|---|
| N-[2-(2,3-Dihydro-1-indolyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamide |  | 435 | 605 |
| N-[2-(3,4-Dihydro-6-methyl-2H-quinol-1-yl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 463 | 606 |
| N-[1-(3-Benzofuranyl)-1-methylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl]oxalamide |  | 420 | 607 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-3-(4-phenoxypiperidino)propyl]oxalamide |  | 507 | 608 |
| N-[2-(1-Butyryl-4-piperidinyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl)phenyl] oxalamide |  | 471 | 609 |
| N-[2-[1-(Methanesulfonyl)-4-piperidinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl) phenyl]oxalamide |  | 479 | 610 |
| N-[2-[1-(Benzenesulfonyl)-4-piperidinyl]-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl) phenyl]oxalamide |  | 541 | 611 |
| N-[2-(1-Isobutyryl-4-piperidinyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(5-oxazolyl) phenyl]oxalamide |  | 471 | 612 |
| tert-Butyl 4-[3-[[[3-methoxy-4-(5-oxazolyl)anilino] oxalyl] amino]-3-methylbutyl]-1-piperidinecarboxylate |  | 515 | 613 |
| N-[3-Methoxy-4-(5-oxazolyl) phenyl]-N'-[1,1-dimethyl-3-(4-piperidinyl)propyl]oxalamide |  | 415 | 614 |

*Examples 428-432:*

Examples 428, 431 and 432 of table 1i were prepared in a manner analogues to that described for example 408 in table 1g but using N-[3-methoxy-4-(4-oxazoyl)phenyl oxalamic acid or N-[3-methoxy-4-(2-methyl-4-oxazoyl)phenyl oxalamic acid in place of N-[3-methoxy-4-(5-oxazoyl)phenyl oxalamic acid for the coupling step.

Examples 429 and 430 of table 1i were prepared by analogues procedures to those described for the preparation of the compounds of table 1f.

table 1i

| Name | Structure | MS(ES) $(M+H)^+$ | Ex No |
|---|---|---|---|
| N-[3-Methoxy-4-(4-oxazolyl)phenyl]-N'-[1,1-dimethyl-2-(4-phenyl-1-piperazinyl)ethyl]oxalamide |  | 478 | 428 |
| N-[2-(4-Benzyloxyphenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(4-oxazolyl)phenyl]oxalamide |  | 500 | 429 |
| N-[2-(4-Hydroxyphenyl)-1,1-dimethylethyl]-N'-[3-methoxy-4-(4-oxazolyl)phenyl]oxalamide |  | 410 | 430 |
| N-[3-Methoxy-4-(4-oxazolyl)phenyl]-N'-[2-[4-(4-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide |  | 508 | 431 |
| N-[3-Methoxy-4-(2-methyl-4-oxazolyl)-phenyl]-N'-[2-[4-(4-methoxyphenyl)-1-piperazinyl]-1,1-dimethylethyl]oxalamide |  | 522.4 | 432 |

The features disclosed in the foregoing description, or the following claims, or the accompanying drawings, expressed in their specific forms or in terms of a means for performing the disclosed function, or a method or process for attaining the disclosed result, as appropriate, may, separately, or in any combination of such features, be utilised for realising the invention in diverse forms thereof.